

1633
#11/108
116/02
1600
P.5

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/585,645

DATE: 12/11/2001

TIME: 15:51:51

Input Set : A:\ES.txt

Output Set: N:\CRF3\12112001\I585645.raw

ENTERED

TECH CENTER 1600/2900

JAN 03 2001

RECEIVED

3 <110> APPLICANT: Zoghbi, Huda
4 Ben-Arie, Nissim
5 Bellen, Hugo
6 Bermingham, Nessim
7 Hassan, Bassem
9 <120> TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR THE THERAPEUTIC USE OF AN ATONAL-ASSOCIATED
10 SEQUENCE FOR DEAFNESS, OSTEOARTHRITIS, AND ABNORMAL CELL PROLIFERATION
12 <130> FILE REFERENCE: HO-P01899US2/09906355/OTA 99-47
14 <140> CURRENT APPLICATION NUMBER: US 09/585,645
15 <141> CURRENT FILING DATE: 2000-06-01
17 <150> PRIOR APPLICATION NUMBER: US 60/137,060
18 <151> PRIOR FILING DATE: 1999-06-01
20 <150> PRIOR APPLICATION NUMBER: US 60/176,993
21 <151> PRIOR FILING DATE: 2000-01-19
23 <150> PRIOR APPLICATION NUMBER: PCT/US00/15410
24 <151> PRIOR FILING DATE: 2000-06-01
26 <160> NUMBER OF SEQ ID NOS: 69
28 <170> SOFTWARE: PatentIn version 3.0
30 <210> SEQ ID NO: 1
31 <211> LENGTH: 1065
32 <212> TYPE: DNA
33 <213> ORGANISM: HUMAN
35 <400> SEQUENCE: 1
36 atgtcccgcg tgcgtcatgc agaagagtgg gctgaagtga aggagttggg agaccaccat 60
38 cgccagcccc agccgcaccca tctcccgcga cgcgcgcgcg ccctcctgga acctgcaact 120
40 ttgcaggcga gagagcatcc cgtctacccg cctgagctgt ccctcctgga cagcacogac 180
42 ccacgcgcct ggcgtgctcc cactttgcag ggcattctga cggcacgcgc cgccagtat 240
44 ttgctacatt ccccggagct ggggtgcctca gaggccgctg cgccccggga cgaggtggac 300
46 ggccgggggg agctggttaag gaggagcagc ggccggtgcca gcagcagcaa gagccccggg 360
48 ccggtgaaag tgcgggaaca gctgtgcaag ctgaaaggcg ggggtggtggt agacgagctg 420
50 ggctgcagcc gccaacgggc cccttcacgc aaacagggtga atggggtgca gaagcagaga 480
52 cggctagcag ccaacgccag ggagcggcgc aggatgcatg ggctgaacca cgccttcgac 540
54 cagctgcgca atgttatccc gtcgttcaac aacgacaaga agctgtccaa atatgagacc 600
56 ctgcagatgg cccaaatcta catcaacgcc ttgtccgagc tgctacaaac gccacgcgga 660
58 ggggaacagc caccgccgcc tccagcctcc tgcaaaagcg accaccacca ccttcgcacc 720
60 gcggcctcct atgaaggggg cgcgggcaac gcgaccgcag ctgggggtca gcaggcttcc 780
62 ggaggggagcc agcggccgac cccgcccggg agttgccgga ctgccttctc agccccagct 840
64 tctgcgggag ggtactcggg gcagctggac gctctgcaact tctcgacttt cgaggacagc 900
66 gccctgacag cgatgatggc gcaaaagaat ttgtctcctt ctctccccgg gagcatcttg 960
68 cagccagtgc aggaggaaaa cagcaaaact tcgcctcggg cccacagaag cgacggggaa 1020
70 ttttcccccc attcccatta cagtgactcg gatgaggcaa gttag 1065
73 <210> SEQ ID NO: 2
74 <211> LENGTH: 354
75 <212> TYPE: PRT
76 <213> ORGANISM: HUMAN
78 <400> SEQUENCE: 2
80 Met Ser Arg Leu Leu His Ala Glu Glu Trp Ala Glu Val Lys Glu Leu

RAW SEQUENCE LISTING

DATE: 12/11/2001

PATENT APPLICATION: US/09/585,645

TIME: 15:51:51

Input Set : A:\ES.txt

Output Set: N:\CRF3\12112001\I585645.raw

```

81 1          5          10          15
83 Gly Asp His His Arg Gln Pro Gln Pro His His Leu Pro Gln Pro Pro
84          20          25          30
86 Pro Pro Pro Gln Pro Pro Ala Thr Leu Gln Ala Arg Glu His Pro Val
87          35          40          45
89 Tyr Pro Pro Glu Leu Ser Leu Leu Asp Ser Thr Asp Pro Arg Ala Trp
90          50          55          60
92 Leu Ala Pro Thr Leu Gln Gly Ile Cys Thr Ala Arg Ala Ala Gln Tyr
93 65          70          75          80
95 Leu Leu His Ser Pro Glu Leu Gly Ala Ser Glu Ala Ala Ala Pro Arg
96          85          90          95
98 Asp Glu Val Asp Gly Arg Gly Glu Leu Val Arg Arg Ser Ser Gly Gly
99          100          105          110
101 Ala Ser Ser Ser Lys Ser Pro Gly Pro Val Lys Val Arg Glu Gln Leu
102          115          120          125
104 Cys Lys Leu Lys Gly Gly Val Val Val Asp Glu Leu Gly Cys Ser Arg
105          130          135          140
107 Gln Arg Ala Pro Ser Ser Lys Gln Val Asn Gly Val Gln Lys Gln Arg
108 145          150          155          160
110 Arg Leu Ala Ala Asn Ala Arg Glu Arg Arg Met His Gly Leu Asn
111          165          170          175
113 His Ala Phe Asp Gln Leu Arg Asn Val Ile Pro Ser Phe Asn Asn Asp
114          180          185          190
116 Lys Lys Leu Ser Lys Tyr Glu Thr Leu Gln Met Ala Gln Ile Tyr Ile
117          195          200          205
119 Asn Ala Leu Ser Glu Leu Leu Gln Thr Pro Ser Gly Gly Glu Gln Pro
120          210          215          220
122 Pro Pro Pro Pro Ala Ser Cys Lys Ser Asp His His His Leu Arg Thr
123 225          230          235          240
125 Ala Ala Ser Tyr Glu Gly Gly Ala Gly Asn Ala Thr Ala Ala Gly Ala
126          245          250          255
128 Gln Gln Ala Ser Gly Gly Ser Gln Arg Pro Thr Pro Pro Gly Ser Cys
129          260          265          270
131 Arg Thr Arg Phe Ser Ala Pro Ala Ser Ala Gly Gly Tyr Ser Val Gln
132          275          280          285
134 Leu Asp Ala Leu His Phe Ser Thr Phe Glu Asp Ser Ala Leu Thr Ala
135          290          295          300
137 Met Met Ala Gln Lys Asn Leu Ser Pro Ser Leu Pro Gly Ser Ile Leu
138 305          310          315          320
140 Gln Pro Val Gln Glu Glu Asn Ser Lys Thr Ser Pro Arg Ser His Arg
141          325          330          335
143 Ser Asp Gly Glu Phe Ser Pro His Ser His Tyr Ser Asp Ser Asp Glu
144          340          345          350
146 Ala Ser
149 <210> SEQ ID NO: 3
150 <211> LENGTH: 420
151 <212> TYPE: DNA
152 <213> ORGANISM: MOUSE
154 <400> SEQUENCE: 3

```

RAW SEQUENCE LISTING

DATE: 12/11/2001

PATENT APPLICATION: US/09/585,645

TIME: 15:51:51

Input Set : A:\ES.txt

Output Set: N:\CRF3\12112001\I585645.raw

```

155 tcgtcccacg cgtccgcgcc aagcccgcgg cgcggaggac accgtgctcg gttccgggct      60
157 gcggggacat tcccggacac acaccggagc agcagctgcg ccgcgacaca tctggagccg      120
159 cgtaggatgt tcgtcaaata tgagactctg gagttgaagg aggaagagga ggtactgatg      180
161 ctgctgggct cggcttcccc ggctcggcg accctgacct cgatgtctc cagcgcggac      240
163 gaggaggagg acgaggagct gcgcggccg ggctccgcgc gtgggcagcg tggagcggaa      300
165 gccgggcagg gggcgcaggg cagtccggcg tcgggtgcct ggggttgccg gacagggcgg      360
167 ctgctatgca ctgtgcacga gtgctagcgt gtgccgtcgc gctcacgggc cgtctgcaga      420
170 <210> SEQ ID NO: 4
171 <211> LENGTH: 645
172 <212> TYPE: DNA
173 <213> ORGANISM: MOUSE
175 <400> SEQUENCE: 4
176 atggcgctc atcccttggg tgcgctcacc atccaagtgt cccagagac acaacaacct      60
178 tttcccggag cctcggacca cgaagtgtc agttccaatt ccacccacc tagccccact      120
180 ctcatacctt gggactgtc cgaagcagaa gtgggtgact gccgaggac ctcgaggaag      180
182 ctccgcgccc gacgcggagg gcgcaacagg cccaagagcg agttggcact cagcaaacag      240
184 cgaagaagcc ggcgcaagaa ggccaatgat cgggagcgca atcgcatgca caacctcaac      300
186 tcggcgctgg atgcgctgcg cgggtgtcctg cccaccttcc cggatgacgc caaacttaca      360
188 aagatcgaga cctgcgctt cgcacacaac tacatctggg cactgactca gacgtgcgc      420
190 atagcggacc acagcttcta tggcccggag cccctgtgc cctgtggaga gctggggagc      480
192 cccggagggtg gctccaacgg ggactggggc tctatctact cccagctctc ccaagcgggt      540
194 aacctgagcc ccacggcctc attggaggaa ttccctggcc tgcagggtgc cagctcccca      600
196 tcctatctgc tcccgggagc actgggtgtt tcagacttct tgtga                                645
199 <210> SEQ ID NO: 5
200 <211> LENGTH: 214
201 <212> TYPE: PRT
202 <213> ORGANISM: MOUSE
204 <400> SEQUENCE: 5
206 Met Ala Pro His Pro Leu Asp Ala Leu Thr Ile Gln Val Ser Pro Glu
207 1 5 10 15
209 Thr Gln Gln Pro Phe Pro Gly Ala Ser Asp His Glu Val Leu Ser Ser
210 20 25 30
212 Asn Ser Thr Pro Pro Ser Pro Thr Leu Ile Pro Arg Asp Cys Ser Glu
213 35 40 45
215 Ala Glu Val Gly Asp Cys Arg Gly Thr Ser Arg Lys Leu Arg Ala Arg
216 50 55 60
218 Arg Gly Gly Arg Asn Arg Pro Lys Ser Glu Leu Ala Leu Ser Lys Gln
219 65 70 75 80
221 Arg Arg Ser Arg Arg Lys Lys Ala Asn Asp Arg Glu Arg Asn Arg Met
222 85 90 95
224 His Asn Leu Asn Ser Ala Leu Asp Ala Leu Arg Gly Val Leu Pro Thr
225 100 105 110
227 Phe Pro Asp Asp Ala Lys Leu Thr Lys Ile Glu Thr Leu Arg Phe Ala
228 115 120 125
230 His Asn Tyr Ile Trp Ala Leu Thr Gln Thr Leu Arg Ile Ala Asp His
231 130 135 140
233 Ser Phe Tyr Gly Pro Glu Pro Pro Val Pro Cys Gly Glu Leu Gly Ser
234 145 150 155 160
236 Pro Gly Gly Gly Ser Asn Gly Asp Trp Gly Ser Ile Tyr Ser Pro Val

```

RAW SEQUENCE LISTING

DATE: 12/11/2001

PATENT APPLICATION: US/09/585,645

TIME: 15:51:51

Input Set : A:\ES.txt

Output Set: N:\CRF3\12112001\I585645.raw

```

237          165          170          175
239 Ser Gln Ala Gly Asn Leu Ser Pro Thr Ala Ser Leu Glu Glu Phe Pro
240          180          185          190
242 Gly Leu Gln Val Pro Ser Ser Pro Ser Tyr Leu Leu Pro Gly Ala Leu
243          195          200          205
245 Val Phe Ser Asp Phe Leu
246          210
248 <210> SEQ ID NO: 6
249 <211> LENGTH: 1412
250 <212> TYPE: DNA
251 <213> ORGANISM: MOUSE
253 <400> SEQUENCE: 6
254 cgtgctcggg tccgggctgc ggggacattc ccggacacac accggagcag cagctgcgcc      60
256 gcgacacatc tggagccgcg taggatgttc gtcaaactctg agactctgga gttgaaggag      120
258 gaagaggagg tactgatgct gctgggctcg gcttcccccg cctcggcgac cctgacccccg      180
260 atgtcctcca gcgcggacga ggaggaggac gaggagctgc gccggccggg ctccgcgcgt      240
262 gggcagcgtg gaggcgaagc cgggcagggg gtgcagggca gtccggcgtc ggggtgccggg      300
264 ggttgccggc cagggcggct gctgggcctg atgcacgagt gcaagcgctc ccgctcgcgc      360
266 tcacgggccc tctcccagag tgccaagacg gcggagacgg tgcagcgcat caagaagacc      420
268 cgcaggctca aggccaaaca ccgcgagcgc aaccgcatgc acaacctaaa cgcgcgcgtg      480
270 gacgcgctgc gcgagggtgct gcccaccttc cccgaggatg ccaagctcac gaagatcgag      540
272 acgctgcgct tcgcccacaa ttacatctgg gcgctcaccg agactctgcg cctggcggac      600
274 cactgcgcgc gcgcgggtgg cctccagggg gcgctcttca cggaggcggt gctcctgagc      660
276 ccgggagctg cgcctcggcg cagcggggac agcccttctc caccttctc ctggagctgc      720
278 accaacagcc cggcgtcatc ctccaactcc acgtcccatc acagctgcac ttatctgccc      780
280 gctagccccg ggtcagacgt ggactactgg cagccccac ctccggagaa gcctcgttat      840
282 gcgcctcacc tgcccctcgc cagggactgt atctagagct gcgggtctcc ctctctcgtc      900
284 ctctaccggc cctcttccc atccttctcc cgcctcacc cctccacgcc ccggaactca      960
286 ctccacagag cagagggtggc ccttgcaatc ccctcggcgg ctggtgcatt cgggggtgga      1020
288 gaccagctct ggtttattga agatgtgagg atttatggtc aaagaggact atggcgtgtg      1080
290 ggagtggggg ctggcgtggg gaacctcgta agactgtaaa agacactgag aaaaagtacc      1140
292 ataactaacg agtgtgcaga gcagactgac gctcctcccc tctctcagag ctgctggagg      1200
294 agaactccgg gcaggcagtt cgtgtgaatc tctcagaggg aatgcaactg gtccctgtga      1260
296 tcttttcacc ttogtttcta catagagatg ttaatgtcag tcgaaagaaa tgtattttag      1320
298 catctgaatg aatttactgg taataatatt atccacacat ttgcaatggc tggcatctgc      1380
300 tctattccca ttgctgtctg caggctgtgg ga
303 <210> SEQ ID NO: 7
304 <211> LENGTH: 263
305 <212> TYPE: PRT
306 <213> ORGANISM: MOUSE
308 <400> SEQUENCE: 7
310 Met Phe Val Lys Ser Glu Thr Leu Glu Leu Lys Glu Glu Glu Glu Val
311 1          5          10          15
313 Leu Met Leu Leu Gly Ser Ala Ser Pro Ala Ser Ala Thr Leu Thr Pro
314          20          25          30
316 Met Ser Ser Ser Ala Asp Glu Glu Glu Asp Glu Glu Leu Arg Arg Pro
317          35          40          45
319 Gly Ser Ala Arg Gly Gln Arg Gly Ala Glu Ala Gly Gln Gly Val Gln
320          50          55          60

```

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/585,645

DATE: 12/11/2001

TIME: 15:51:51

Input Set : A:\ES.txt

Output Set: N:\CRF3\12112001\I585645.raw

```

322 Gly Ser Pro Ala Ser Gly Ala Gly Gly Cys Arg Pro Gly Arg Leu Leu
323 65                               70                               75                               80
325 Gly Leu Met His Glu Cys Lys Arg Arg Pro Ser Arg Ser Arg Ala Val
326                               85                               90                               95
328 Ser Arg Gly Ala Lys Thr Ala Glu Thr Val Gln Arg Ile Lys Lys Thr
329                               100                              105                              110
331 Arg Arg Leu Lys Ala Asn Asn Arg Glu Arg Asn Arg Met His Asn Leu
332                               115                              120                              125
334 Asn Ala Ala Leu Asp Ala Leu Arg Glu Val Leu Pro Thr Phe Pro Glu
335                               130                              135                              140
337 Asp Ala Lys Leu Thr Lys Ile Glu Thr Leu Arg Phe Ala His Asn Tyr
338 145                               150                              155                              160
340 Ile Trp Ala Leu Thr Glu Thr Leu Arg Leu Ala Asp His Cys Ala Gly
341                               165                              170                              175
343 Ala Gly Gly Leu Gln Gly Ala Leu Phe Thr Glu Ala Val Leu Leu Ser
344                               180                              185                              190
346 Pro Gly Ala Ala Leu Gly Ala Ser Gly Asp Ser Pro Ser Pro Pro Ser
347                               195                              200                              205
349 Ser Trp Ser Cys Thr Asn Ser Pro Ala Ser Ser Ser Asn Ser Thr Ser
350                               210                              215                              220
352 Pro Tyr Ser Cys Thr Leu Ser Pro Ala Ser Pro Gly Ser Asp Val Asp
353 225                               230                              235                              240
355 Tyr Trp Gln Pro Pro Pro Pro Glu Lys His Arg Tyr Ala Pro His Leu
356                               245                              250                              255

```

358 Pro Leu Ala Arg Asp Cys Ile

359 260

361 <210> SEQ ID NO: 8

362 <211> LENGTH: 1957

363 <212> TYPE: DNA

364 <213> ORGANISM: MOUSE

366 <400> SEQUENCE: 8

```

367 gatacacaca gatctagagg ctccaggaga cgatgcgaca ctcagcctga aaagatttgg 60
369 aagatccaaa atgaaaactg attattgaat gaaattaaaa cctaaggtaa attaaggtta 120
371 aagaaccatg ttaacactac cgtttgacga gtctgtcgta atgcccgat cccagatgtg 180
373 cagaaagtgt gctagacaat gtgaggacca gaaacaaatt aagaaaccag agagctttcc 240
375 aaaacaagtt gtccttcgag gaaagagcat taaaagggcc cctggagaag aaaccgagaa 300
377 agaagaggag gaagaagaca gagaggaaga agatgagaat ggcttgcca gaaggagggg 360
379 gctcaggaaa aaaaagacca ccaaactacg actggaaagg gtcaagttca ggagacagga 420
381 agctaattgc cgcgagagga accggatgca cggcctcaat gatgctctgg acaatttgcg 480
383 aaaagtggtc ccctgttact ctaaaacca aaaactgtcc aaaatagaaa ctttacgact 540
385 ggccaaaaat tacatctggg cactttctga aattctgagg attggcaaga gaccggatct 600
387 gctcacgttc gtccaaaact tatgcaaagg tctttccag ccaactacaa acttggtggc 660
389 aggtctgctta cagctcaacg ccagaagttt cctgatgggt caggggtggg aggctgccca 720
391 ccacacaagg tcacctact ccacattcta ccacctac cacagccctg agctggccac 780
393 tccccagggg catgggactc ttgataatc caagtocatg aaaccctaca attactgcag 840
395 tgcatatgaa tcctttctatg aaagtacctc ccctgagtgt gccagccctc agtttgaagg 900
397 tcccttaagt cctcccccaa ttaactataa tgggatattt tccctgaagc aagaagaaac 960
399 cttggactat ggcaaaaatt acaattatgg catgcattac tgtgcagtgc caccaggggg 1020
401 tccccttggg caggggtgcc tgttcaggtt gccaccgcac agccacttcc cttacgactt 1080

```

Use of n and / or Xaa has been detected in the Sequence Listing. Review the Sequence Listing to ensure a corresponding explanation is present in the <220> to <223> fields of each sequence using n or Xaa.

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/585,645

DATE: 12/11/2001

TIME: 15:51:52

Input Set : A:\ES.txt

Output Set: N:\CRF3\12112001\I585645.raw

L:754 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:13
L:855 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:16
L:2767 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:57
L:2769 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:57
L:2771 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:57
L:2866 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:59